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Claims 1-23 were pending. By way of this response, claims 3 and 14 have been canceled, and claims 1, 4 and 23 have been amended. Accordingly, claims 1, 2, 4-13, and 15-23 remain pending.

Item 1 of the Office Action - Rejections Under 35 U.S.C. § 102

Claims 1-6, 14-17, and 21 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Neumann (U.S. Pat. No. 4,188,393). Claims 1, 2, 5, 6, 9-17, and 20-21 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by DeSantis Jr. et al. (U.S. Pat. No. 5,811,443, referred to herein as DeSantis).

Applicant has amended claims 1 and 23, as set forth above. Applicant traverses the rejections as they relate to the amended claims.

Neumann discloses a composition containing 5-bromo-6-(2-imidazolin-2-yl-amino)-quinoxaline and stearic acid. Neumann does not disclose these components in a complex, let alone, a composition in which the stearic acid is provided in an amount to enhance the movement of the 5-bromo-6-(2-imidazolin-2-yl-amino)-quinoxaline across a lipid membrane, as recited in the present claims.

DeSantis discloses a composition containing a clonidine derivative and a prostaglandin. DeSantis does not disclose the clonidine derivative and the prostaglandin as forming a complex,

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let alone, prostaglandin being effective to provide enhanced movement across a lipid membrane, as recited in the present claims.

Accordingly, applicant submits the claims are not anticipated by Neumann or by DeSantis.

Moreover, neither Neumann nor DeSantis suggest the claimed compositions to support a rejection under 35 U.S.C. § 103.

In view of the above, applicant submits that the present claims, that is claims 1, 2, 4-13, and 15-23, are not anticipated by, and are unobvious from and patentable over, Neumann and DeSantis under 35 U.S.C. § 102(b).

Item 2 of the Office Action - Rejections Under 35 U.S.C. § 103

Claims 7, 8, 18, 19, 22, and 23 have been rejected as allegedly unpatentable over Anderson (WO 00/44355). The Office Action states that it would have been obvious to a person of ordinary skill in the art to substitute one fatty acid for another in the absence of evidence to the contrary (Office Action, page 3).

Applicant respectfully disagrees and respectfully traverses the rejection. Among other things, applicant submits that the Examiner has not met the burden of proof to establish a prima facie case of obviousness. The Office Action fails to indicate where in the prior art a suggestion or motivation is provided to

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modify the teachings of Anderson to obtain the claimed compositions. Absent such an indication, applicant submits that the rejections under 35 U.S.C. § 103 cannot be maintained. The motivation or suggestion to support a rejection under 35 U.S.C. § 103 must be clear and particular (*In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999), emphasis added), and "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed" (*In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000)). Applicant respectfully submits that the prior art fails to provide a clear and particular showing that one of ordinary skill in the art would have been motivated to modify the teachings of Anderson to obtain the claimed compositions. Absent such a clear and particular indication, the rejections under 35 U.S.C. § 103 cannot be maintained.

In addition, applicant submits that the claimed compositions are not obvious over Anderson. The present claims recite a fatty acid component present in an amount to enhance the movement of the quinoxaline component across lipid membranes. The amount of the fatty acid component in the complex advantageously provides enhanced pharmacokinetic properties and reduced irritation (for example, see page 4, 4<sup>th</sup> full paragraph; and page 11, 3<sup>rd</sup> full paragraph). This is in contrast to the teachings of Anderson which indicate that the moxonidine salts have reduced pharmacokinetic properties (e.g., sustained release).

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The Office Action also states that the data in Table I are confusing because the data show higher sedation scores for brimonidine tartrate over the claimed complexes. Applicant respectfully disagrees that the data are confusing. Applicant submits that the data confirm some of the unexpected results achieved with the claimed compositions as compared to compositions without the fatty acid components. For example, as explained previously, the claimed compositions provide desired therapeutic effects without the sedative effects associated with brimonidine tartrate.

In view of the above, applicant submits that the present claims, and in particular, claims 7, 8, 18, 19, 22, and 23 are unobvious from and patentable over, Anderson under 35 U.S.C. § 103.

Each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present compositions including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

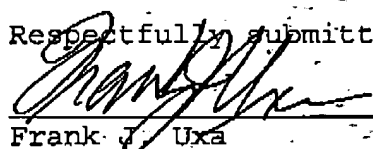
In conclusion, applicant has shown that the present claims are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 1, 2,

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4-13, and 15-23 are allowable. Therefore, applicant requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Date: 2/4/03

Respectfully submitted,

  
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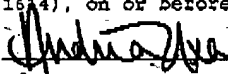
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## CERTIFICATE OF FACSIMILE TRANSMISSION

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Andrea Uxa, Assistant

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 3 and 14 have been canceled.

Claims 1, 4, and 23 have been amended as follows:

1. (2x Amended) A composition comprising:  
[an alpha-2-adrenergic agonist] a quinoxaline  
component, and  
a fatty acid component, the fatty acid component being  
present in a complex with the alpha-2-adrenergic agonist; the  
complex remaining substantially intact in an aqueous environment  
and the fatty acid component being present in an amount  
effective to enhance movement of the quinoxaline component  
across a lipid membrane relative to a substantially identical  
quinoxaline component without a fatty acid component.

4. (Amended) A composition of claim [3] 1 wherein the  
quinoxaline component is selected from the group consisting of  
quinoxaline, (2-imidazolyl-2-ylamino) quinoxaline, 5-bromo-6-(2-  
imidazolyl-2-ylamino) quinoxaline, and derivatives thereof and  
mixtures thereof.

23. (2x Amended) A composition comprising:  
5-bromo-6-(2-imidazolyl-2-ylamino) quinoxaline; and  
a [linolenic] linoleic acid component;  
wherein the 5-bromo-6-(2-imidazolyl-2-ylamino)  
quinoxaline is present in a complex with the linoleic acid

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component, the complex substantially remains intact in an aqueous environment and the linoleic acid component being present in an amount effective to enhance movement of the 5-bromo-6-(2-imidazolyl-2-ylamino) quinoxaline across a lipid membrane relative to 5-bromo-6-(2-imidazolyl-2-ylamino) quinoxaline without a fatty acid component.